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Seth Eckstein
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Signature of person mailing correspondence

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Sannicolo et al.	Art Unit:	1621
Serial No.:	10/506,305	Examiner:	Porfirio Nazario Gonzalez
Filed:	September 1, 2004	Customer No.:	21559
Confirmation No.:	8330		
Title:	Metallic Catalysts for Chemo-, Regio- and Stereoselective Reactions, and Corresponding Precursors		

Mailstop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL OF CERTIFIED TRANSLATION

In reference to the Office Action that was mailed in connection with the above-captioned patent application on April 13, 2007, and the Reply filed on July 13, 2007, Applicants enclose herewith an original certified copy of the translation of Italian application MI2002A000415, filed March 1, 2002, a PDF copy of which was submitted with the Reply.

Although no fees are believed to be due, if there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: July 17, 2007

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SEAL

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SEAL OF THE ABOVE MINISTRY

Authentication of copy of documents concerning the Patent application for INDUSTRIAL INVENTION No. MI2002A000415

It is hereby certified that the attached copy is the true copy of the original documents filed with the above mentioned patent application whose data are shown in the enclosed filing certificate.

Rome, date

THE DIRECTOR
OF THE DIVISION

(signature)

SEAL

FORM A DUTY STAMP

TO THE MINISTRY OF INDUSTRY COMMERCE AND HANDICRAFT
Main Patent Office - ROME
Patent Application for Industrial Invention, filing of reserves,
advanced opening to public inspection

A. Applicant (1) G.S. Physical person
1) Name CHEMI S.p.A. code 00148870603
Residence CINISELLO BALSAMO (Province of MILANO)

Name G.S.
Residence code

B. APPLICANT'S REPRESENTATIVE BEFORE M.P.O.
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Address Corso di Porta Vittoria 9 city Milan zip code 20122 province MI

C. ELECTED DOMICILE OF THE ADDRESSEE As above
Address city code prov

D. TITLE proposed class, (sec./cl./ucl.) group/subgroup

Metallic catalysts for chemo-, regio- and stereoselective reactions, and corresponding precursors

ADVANCED OPENING TO PUBLIC INSPECTION yes___ no_x__
in presence of amendment request: date no. of ref.:

E. NAMED INVENTORS

surname, name	surname, name
1) SANNICOLO' Francesco	3) BENICORI Tiziana
2) PICCOLO Oreste	4) SADA Mara

F. PRIORITY
Country or Exhibition Type of Priority Appln. No. Appln. date Encl(yes/res)

1) NONE

G. CENTRE FOR COLLECTING MICROORGANISMS'CULTURES, denomination

H. SPECIAL NOTES
None

ENCLOSED DOCUMENTS

					RESERVES DISSOLUTION
Specimen No.					date No. of ref.
Doc. 1) 2	prov.	no. sheets 38	abstract with main drawing, spec. and claims (compulsory 1 copy)		
Doc. 2) 0	prov.	no. sheets 00	drawing (compulsory if cited in description, 1 copy)		
Doc. 3) 1	res.		power of attorney or reference attorney		
Doc. 4) 0	res.		designation of inventor		
Doc. 5) 0	res.		priority document with Italian translation		comparison single priority
Doc. 6) 0	res.		authorisation or assignment deed		
Doc. 7) 0	res.		complete name of the applicant		

PAYMENT RECEIPT OF Euro TWOHUNDREDNINETYONE/80 compulsory
filed in on 01/03/2002

The applicant's signature Gemma Gervasi
(signature)

follows yes/no YES
We required certified copy of the present deed yes/no YES

CHAMBER OF COMMERCE INDUSTRY HANDICRAFT AND AGRICOLTURE OF MILAN code 15
FILING CERTIFICATE Application no. MI2002A000415 Reg. A
The year 2002 the 1st day of the month of March

The above mentioned applicant(s) has(have) presented to me undersigned the present application consisting of no. 01 additional sheets for the grant of the above patent.

I. DIFFERENT NOTES OF THE RECORDING OFFICER THE REPRESENTATIVE, HAVING BEEN INFORMED OF THE CONTENT OF CIRCULAR NO 423 OF 1 MARCH 2002, FILES THE APPLICATION WITHOUT POWER OF ATTORNEY
none

THE DEPOSITER
(signature)

THE RECORDING OFFICER
(signature)
SEAL

ADDITIONAL SHEET FORM A

Attached sheet No. 02 of total 02 Appln. No. MI2002A000415 Reg. A

A. APPLICANT

Name G.S.

Residence Code

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Name

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E. NAMED INVENTORS

Surname name Surname name

05 VERRAZZANI Alessandra

06 TOLLIS Simona

07 ULLUCCI Elio

08 DE FERRA Lorenzo

F. PRIORITY

Country or Exhibition Type of Priority Appln. No. Appln. date Encl(yes/res)

RE SERVES DISSOLUTION
date ref. No.

THE APPLICANT'S SIGNATURE

Diego Pallini
(signature)

FORM A

ABSTRACT OF THE INVENTION TOGETHER WITH MAIN DRAWING, SPECIFICATIONS AND CLAIMS

Application No. MI2002A000415 Filing date 01/03/2002

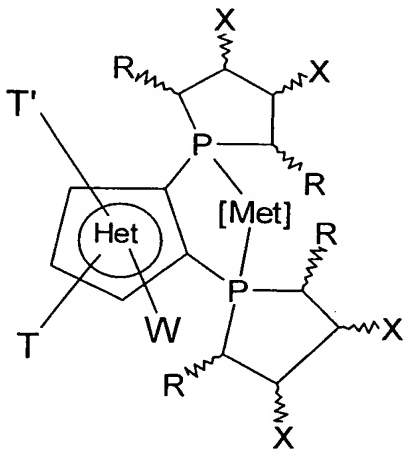
Patent No. Date of grant

D. TITLE

"Metallic catalysts for chemo-, regio- and stereoselective reactions, and corresponding precursors"

L. ABSTRACT

Metallic catalysts of the general formula (I) and their precursors, suitable for chemo- regio- and stereoselective reactions, derived from ortho-*bis*(1-phospholanyl)-heteroarenes. The new catalysts are characterized by the presence of two homomorphic phospholanic rings set in adjacent positions of an aromatic pentatomic heterocycle.



M. DRAWING

(I)

Description of the invention for industrial invention having for title:

Metallic catalysts for chemo-, regio- and stereoselective reactions, and corresponding precursors

in the name of CHEMI S.p.A.

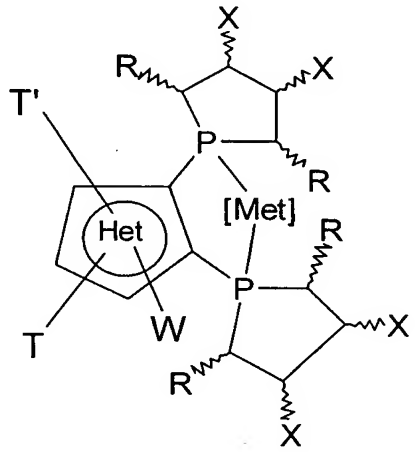
residing in CINISELLO BALSAMO (Province of MILAN)

named inventors: SANNICOLO' Francesco, PICCOLO Oreste, BENINCORI Tiziana, SADA Mara, VERRAZZANI Alessandra, TOLLIS Simona, ULLUCCI Elio, DE FERRA Lorenzo

* * * * *

FIELD OF THE INVENTION

The invention relates to new metallic catalysts and their precursors, characterized by the presence of ortho-*bis*(1-phospholanyl)heteroarenes, of the general formula (I), suitable for chemo- regio- and stereoselective reactions.



(I)

where:

[Met] is a metal chosen from among those of the group Ru, Rh, Ir, Pt, Pd, Ni, Re, and Cu having a state of oxidation n, where n is 0, +1, +2 or +3, and containing possible ancillary co-ligands for completing its state of valence;

represents an aromatic pentatomic heterocycle, containing at least one hetero-atom chosen from among oxygen, sulphur and nitrogen;

T and T', which are the same as or different from one another, are chosen from among hydrogen, a linear C1-C10 alkyl, either cyclic or branched, hydroxyalkyl,

alkoxyalkyl, phenyl, alkylphenyl, naphthyl, alkoxyphenyl, dialkylaminophenyl, carboxyphenyl, carbalkoxyphenyl, or else T and T', taken together, constitute an aromatic carbocyclic ring, which is possibly substituted by one or more alkyl, hydroxy, alkoxy, dialkylamino, carboxy, carbalkoxy or sulphonic groups;

W is a substituent present only when the hetero-atom is nitrogen and is chosen from among H, a linear C1-C10 alkyl, either cyclic or branched, alkoxyalkyl, phenyl, alkylphenyl, naphthyl, alkoxyphenyl, dialkylaminophenyl, carboxyphenyl, carbalkoxyphenyl;

R is chosen from among hydrogen, a linear C1-C10 alkyl, either cyclic or branched, hydroxyalkyl, alkoxyalkyl, phenyl, alkylphenyl;

X is chosen from among H, a linear C1-C10 alkyl, either cyclic or branched, hydroxy, alkoxy, benzyloxy, acyloxy, O-tetrahydropyranyl, O-tetrahydrofuranyl, or else where the two substituents X, taken together with m carbon atoms bound thereto, with m = 1, 2 or 3, form a carbocyclic ring with a total of 5-7 atoms or a saturated heterocyclic ring with 5-7 atoms.

In the case of stereogenic carbon atoms present in the phospholanic ring, in the general formula (I) there are to be understood as included the meso products, the racemic products, and the enantiomerically enriched products, with the limitation, in the case of optically active products, that:

a) the carbon atoms in positions 2' and 5' of the phospholanic rings possess the same absolute configuration with respect to one another;

b) the carbon atoms in positions 3' and 4' of the phospholanic rings possess the same absolute configuration with respect to one another;

The said metallic catalysts are useful in chemo- regio- and stereoselective reactions of hydrogenation, reduction, isomerization, and in reactions of formation of C-C bonds. In particular, as regards the reactions of asymmetrical synthesis, the new catalysts prove particularly useful and efficient in enantioselective reactions of hydrogenation of C=C, C=O, C=N groups, of isomerization of enamines, of formation of C-C bonds, such as, for example, the Heck reaction, the Diels-Alder reaction, allylic substitution and aldolic condensation.

STATE OF THE ART

A large number of chelating phosphinic ligands have been prepared in the last 30

years, and described in patent literature and in scientific publications, as fundamental component of metallic complexes, useful as catalysts for chemo-, regio- and enantioselective reactions. [c.f., for example, H. Brunner, W. Zettlmeier, "Handbook of enantioselective catalysis", VCH, (1993) or I. Ojima *et al.*, "Catalytic Asymmetric Synthesis", Wiley, (2000)]. The concept is, however, commonly and universally accepted that there does not exist a catalyst, and hence a ligand, suitable for every reaction and for every substrate. There thus remains felt the need, in particular for applications of industrial interest, to identify new catalysts suitable both for previously unknown reactions and for improving the results of existing reactions.

In particular, the modern design of new catalysts provided with high capacities of stereoselection tends, more than in the direction of the creation of a single catalyst, even a very efficient one, in the direction of the identification of a modular class of catalysts, i.e., ones provided with a modifiable basic architecture, both in the steric properties and in the electronic properties according to the needs imposed by the reaction and by the substrate.

The former of these two parameters plays a predominant role in regulating the capacity of stereoselection of the catalyst, whilst the latter has a decisive influence on the kinetics of the catalytic process.

The publications and the patents of catalysts containing phosphinic ligands with a phospholanic structure, such as, for example, the documents US 5171892, US 5329015, US 6043396, WO 99/24444, WO 00/11008, have demonstrated the usefulness of such a substructure containing a phosphacycle. However, the limit of such systems is the difficulty of modulating the steric and electronic properties, given that what links the two phospholanic systems (the linker) is an aromatic carbocycle, an alkyl chain or a ferrocenic system. Consequently, the linker not only imposes and imparts a large part of the characteristics of angle of valence or bonding with the metal (the so-called "bite angle"), but contributes to an important extent to the determination of its electronic properties. A further limit is represented by the fact that it is possible to have systems where the two phosphorus atoms are homotopic (ligands with C_2 symmetry), whilst it is known that, in some reactions, metallic catalysts deriving from ligands with C_1 symmetry are more efficient [I.

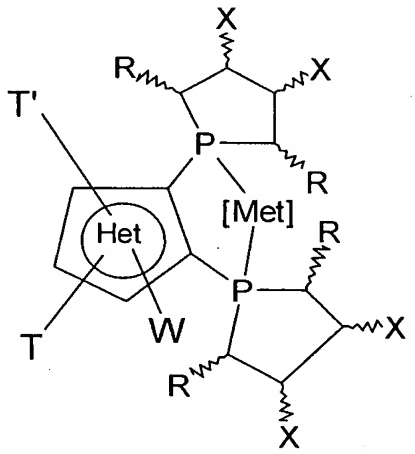
Ojima *et al*, "Catalytic Asymmetric Synthesis", Wiley, (2000)]. The aforesaid inventors, according to the authors of the present patent application, have apparently underestimated the importance of the linker, even though, in actual fact, the results observed in numerous and different reactions and on substrates having different steric and electronic characteristics demonstrate the significant role played by the angle of bonding with the metal, or bite angle, and by the structural flexibility of the catalytic system, which can substantially be put down precisely to what links the two phospholanic systems.

Recently, the present applicant has carried ahead a detailed theoretical and experimental study demonstrating in patents and publications how it is possible to obtain a fine steric and electronic modulation, which is necessary for optimization of chemo, regio- and stereoselective reactions. For instance, in the patent application WO99/52915, there were claimed new ligands with C_1 symmetry containing phospholanic rings as substructures and the corresponding metallic catalysts. A limit of this invention is, however, represented by the fact that the phosphacycles illustrated are set at intervals of 4 carbon atoms part, with the consequent impossibility of obtaining bite angles (P-Metal-P), calculated by computer modelling, of less than 90°. In addition, in the said systems there is present a further source of stereogenicity, represented by the atropoisomeric system, which does not necessarily present the same type of asymmetric induction promoted by the phospholanic systems; i.e., it is possible to encounter cases where the atropoisomeric stereogenicity and the stereogenicity of the phosphacyclic ring go in the same direction ("matched stereoselectivity induction"), but also cases where the effects may go in the opposite direction, with an overall reduction in asymmetric induction ("mismatched stereoselectivity induction"). Proceeding in the search for new, simpler and more effective catalytic systems with C_2 and C_1 symmetry, the present applicant has found the catalysts of the present invention, which, as compared to systems already known, adapt better to the structural and electronic needs of the reagents and of the type of reactions, so enabling the limits of the pre-existing catalytic systems to be overcome. Consequently, the improvement that can be achieved in terms of productivity, and regio-, chemo- and stereoselectivity, makes possible a wider industrial application.

DETAILED DESCRIPTION OF THE INVENTION

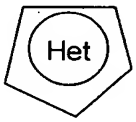
The subject of the present invention are new metallic complexes and their precursors, characterized by the presence of ortho-*bis*(1-phospholanyl) heteroarenes, of the general formula (I), which are suitable for chemo- regio- and stereoselective reactions,

(I)



where:

[Met] is a metal chosen from among those of the group made up of Ru, Rh, Ir, Pt, Pd, Ni, Re, Cu, having a state of oxidation n, where n is 0, +1, +2, or +3, and containing possible ancillary co-ligands for completing its state of valence;



represents an aromatic pentatomic heterocycle, containing at least one hetero-atom chosen from among oxygen, sulphur, and nitrogen;

T and T', which are the same as or different from one another, are chosen from among hydrogen, a linear C1-C10 alkyl, either cyclic or branched, hydroxyalkyl, alkoxyalkyl, phenyl, alkylphenyl, naphthyl, alkoxyphenyl, dialkylaminophenyl, carboxyphenyl, carbalkoxyphenyl, or else T and T', taken together, constitute an aromatic carbocyclic ring, which is possibly substituted by one or more alkyl, hydroxy, alkoxy, dialkylamino, carboxy, carbalkoxy or sulphonic groups;

W is a substituent present only when the hetero-atom is nitrogen and is chosen from among H, a linear C1-C10 alkyl, either cyclic or branched, alkoxyalkyl, phenyl, alkylphenyl, naphthyl, alkoxyphenyl, dialkylaminophenyl, carboxyphenyl, carbalkoxyphenyl;

R is chosen from among hydrogen, a linear C1-C10 alkyl, either cyclic or branched, hydroxyalkyl, alkoxyalkyl, phenyl, alkylphenyl;

X is chosen from among H, a linear C1-C10 alkyl, either cyclic or branched, hydroxy, alkoxy, benzyloxy, acyloxy, O-tetrahydropyranyl, O-tetrahydrofuranyl, or else where the two substituents X, taken together with m carbon atoms bound thereto, with m = 1, 2 or 3, form a carbocyclic ring with a total of 5-7 atoms or a saturated heterocyclic ring with 5-7 atoms.

In the case of stereogenic carbon atoms present in the phospholanic ring, in the general formula (I) there are to be understood as included the meso products, the racemic products, and the enantiomerically enriched products, with the limitation, in the case of optically active products, that:

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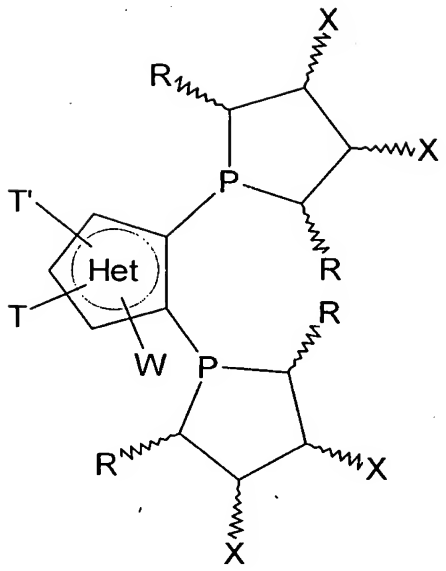
The said metallic catalysts are useful in chemo- regio- and stereoselective reactions of hydrogenation, reduction, isomerization and in reactions of formation of C-C bonds. In particular, as regards the reactions of asymmetrical synthesis, the new catalysts prove particularly useful and efficient in enantioselective reactions of hydrogenation of C=C, C=O, C=N groups, of isomerization of enamines, of formation of C-C bonds, such as, for example, the Heck reaction, the Diels-Alder reaction, allylic substitution and alcoholic condensation.

The catalysts forming the subject of the present invention are prepared starting from the phospholanic ligands of formula (IA)



(IA)

in which T, T', W, X and R have the aforesaid meanings.

The said ligands, on account of the presence of the hetero-aromatic linker, have electronic properties different from those of the corresponding ligands with carbocyclic linker. In addition, according to the relative position of the phosphorus atoms with respect to the hetero-atom present in the linker, the electronic density of the two phosphorus atoms may be differentiated from one another.

Also the steric properties of these ligands vary according to the substituents T, T' and W.

It is thus possible to obtain, with these ligands, catalysts that adapt better to the requirements of the reagents and to the type of the reactions, obtaining, in practice an improved catalytic activity, as demonstrated by kinetic measurements.

Purely by way of example, indicated in what follows are the characteristics of some classes of metallic catalysts containing the ligands of structure (II)-(IV), where Y is chosen from among O, S and N(W), T and W are chosen from between hydrogen and methyl, and where the carbon atoms in positions 2' and 5' of the phospholanic rings have the same absolute configuration with respect to one another:

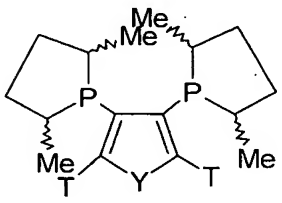
a) the catalysts containing the ligands, where T or else W is methyl, have steric

encumbrance different from those containing ligands where T or else W is hydrogen;

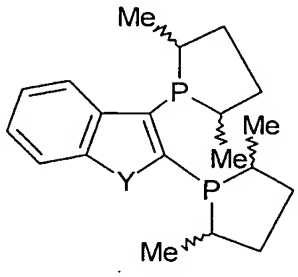
b) the phosphorus atoms of the ligands (II), depending upon the different electronic availability imparted by the heterocycle, when there is present an atom of oxygen, sulphur or else nitrogen, have electronic characteristics that are different from one another, which reflect upon the characteristics of the catalysts that contain them;

c) the ligands (III) contain two phosphorus atoms having different electronic availability;

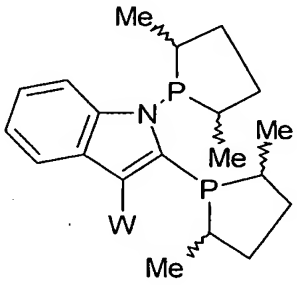
d) the ligands (IV) offer a further possibility of differentiating the steric and electronic characteristics of the phosphorus atoms.



(II)



(III)



(IV)

The said properties (a-d) were hard to obtain or even unobtainable in catalysts containing the phosphacyclic system so far known and enable the previous limitations to be overcome.

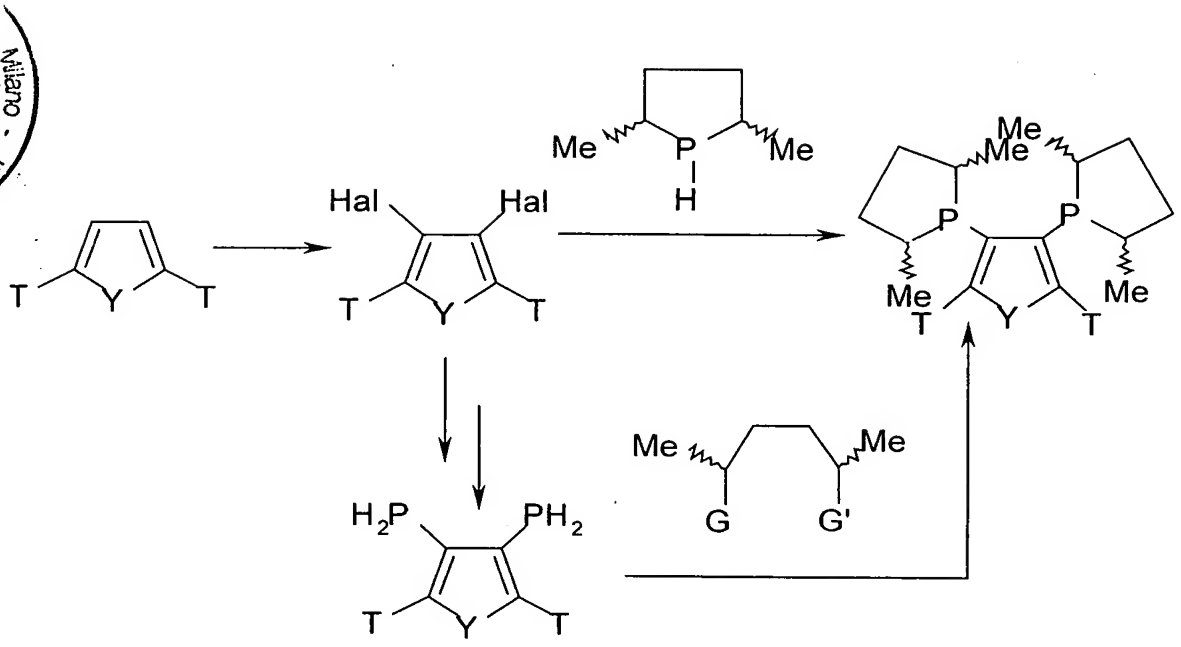
The synthesis of the new ligands (IA) uses reaction schemes in themselves known [c.f., for instance, H. Brunner *et al.*, J. Organomet. Chem. *328*, 71 (1987); M.J. Burk, J. Am. Chem. Soc., *113*, 8518 (1991); M.J. Burk *et al.*, Organometallics *9*, 2653 (1990); M.J. Burk, J. Am. Chem. Soc.,*115*, 10125 (1993); J. Holz *et al.* J. Org. Chem., *63*, 8031 (1998); Y.-Y. Yan and T.V. RajanBabu, J. Org. Chem., *65*, 900 (2000)]. For instance, purely by way of example, some of these ligands may be prepared according to Schemes 1 and 1' (in both schemes, Hal is a halogen atom, and G and G' are a mesylated group, a tosylated group or, taken together, represent the group O-SO_2-O).

In particular, the first reaction of both of the schemes is a halogenation of the

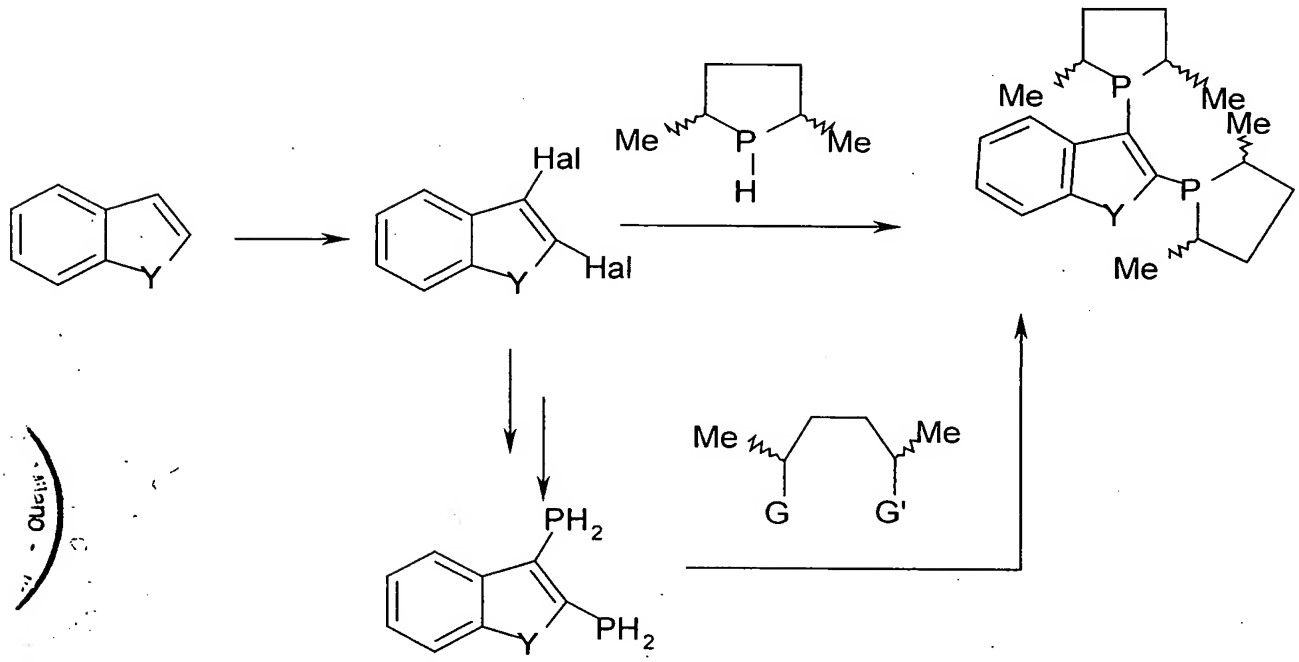
hetero-aromatic ring in positions 3 and 4 or else 2 and 3, respectively. Subsequently, the heteroarene dihalogen may be made to react with a phospholan in the presence of palladium-based catalysts to obtain the desired product.

Alternatively, the heteroarene dihalogen may be made to react with triethyl phosphite to obtain the corresponding *bis*-diethoxyphosphoryl heteroarene, which is subsequently reduced with lithium aluminium hydride to *bis*-diphosphinoheteroarene. Finally, the latter is made to react with bifunctional alkylating agents derived from the hexanediol, such as, for example, the *bis*-methane sulphonates, the *bis*-toluene sulphonates or else with cyclic sulphates, to obtain the desired product. In particular, to obtain a phospholanic ligand in a specific enantiomeric form, it is necessary for the reagents used to have the two stereocentres with the same absolute configuration.

Scheme 1

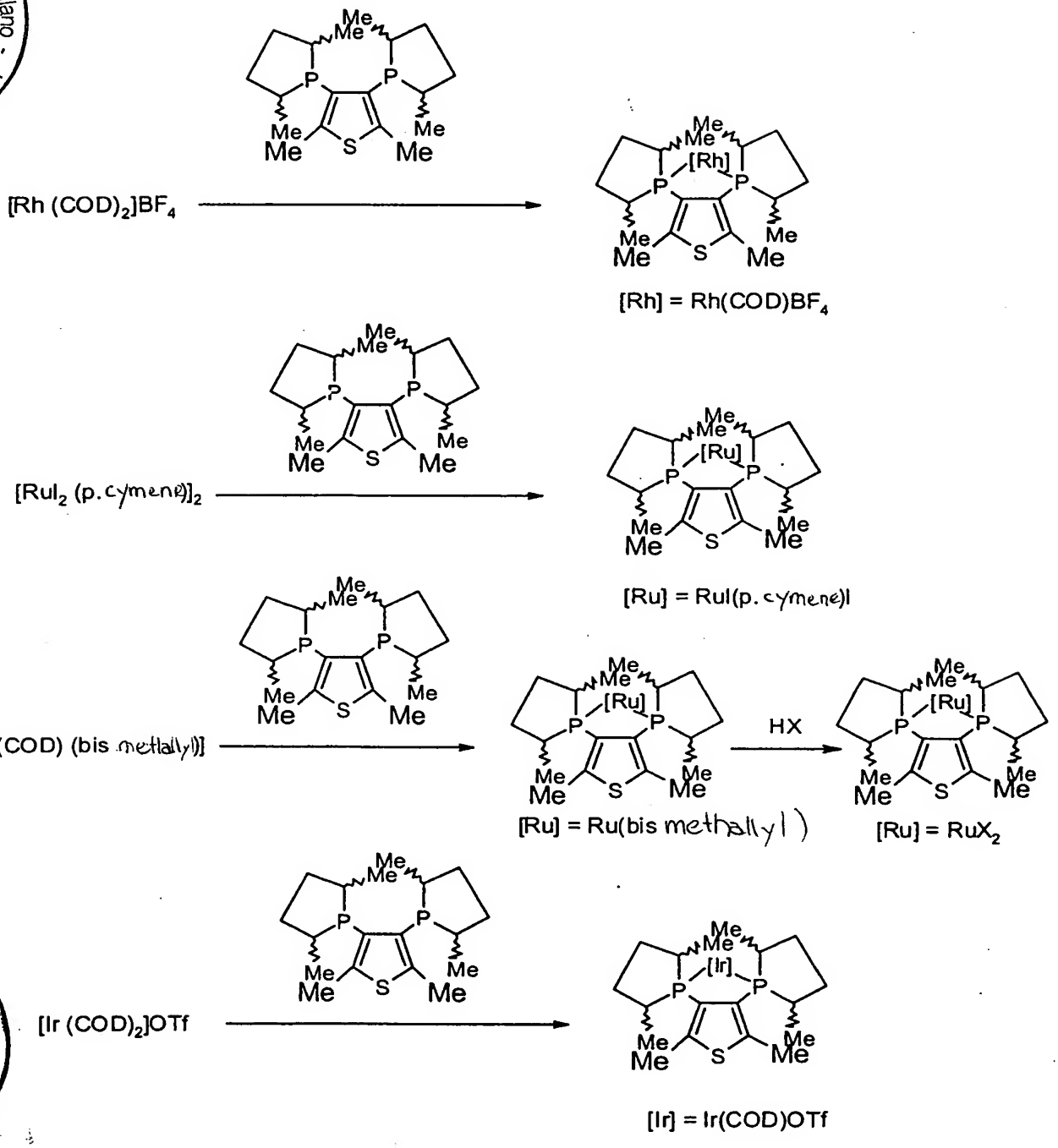


Scheme 1'



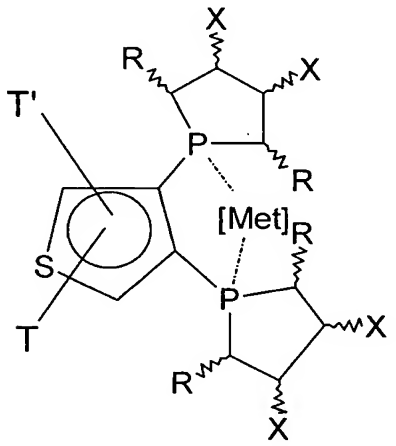
The preparation of the catalysts of formula (I) is conducted using the phospholanic ligands of formula (IA), according to methodologies known to the person skilled in the branch [c.f., for example T.G. Schenck *et al.*, Inorg. Chem. 24, 2334 (1985); and K. Mashima *et al.*, J. Org. Chem., 59, 3064 (1994)]. Shown in Scheme 2, purely by way of example, are the synthetic schemes of some catalysts of formula (I) according to the present invention.

Scheme 2

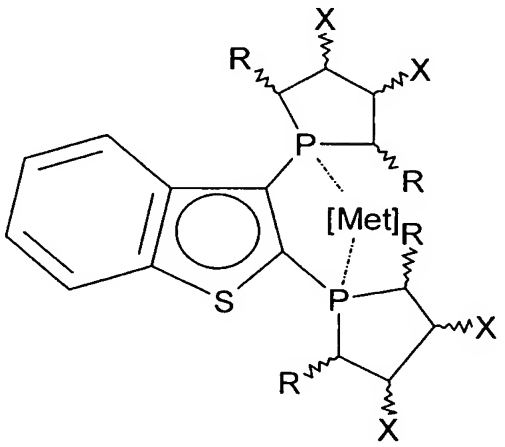

[Rh (COD)2]BF4
[Rh] = Rh(COD)BF4
[RuI2 (p.cymene)]2
[Ru] = RuI(p.cymene)I
[Ru(COD) (bis methallyl)]
[Ru] = Ru(bis methallyl)
HX
[Ru] = RuX2
[Ir (COD)2]OTf
[Ir] = Ir(COD)OTf

The catalysts forming the subject of the present invention have advantageously been applied in regio-, chemo- and stereoselective reactions and in particular in enantioselective reactions of hydrogenation of C=C, C=O, C=N groups, of isomerization of enamines, of formation of C-C bonds, such as, for example, the Heck reaction, the Diels-Alder reaction, allylic substitution and alcoholic condensation.

Amongst the metallic catalysts with a base of Rh, Ru, Ir, Pd, Pt, Re, Ni or Cu, of the general formula (I), there are preferentially selected those containing a thiophenic or benzothiophenic ring of the general formula (V) and (VI), respectively.



(V)

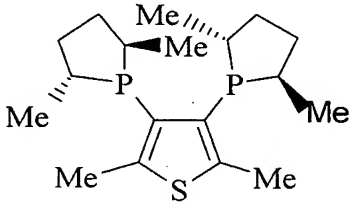


(VI)

Further preferred are the metallic catalysts of formula (V) and (VI), where T and T' are both hydrogen or both methyl, where R is other than hydrogen, and the two stereocentres present in positions 2' and 5' of the phospholanic rings have, with respect to one another, the same absolute configuration, and where the two stereocentres in positions 3' and 4' of the phospholanic rings, if present, have, with respect to one another, the same absolute configuration.

As illustration of the present invention the following non-limiting examples are provided.

Example 1. Synthesis of (R,R) 2,5–dimethyl-[3,4 *bis*(2',5'-dimethylphospholanyl)]-thiophene



Stage a: synthesis of 2,5-dimethyl-3,4-diiodo-thiophene

Into a 2-L four-necked flask, provided with mechanical stirrer, thermometer and coolant, there were introduced 80 mL of H_2O, 20 g of $NaIO_3$, 26 g of I_2, 7 mL of AcOH, 60 g of 3-iodo-2,5-dimethylthiophene, dissolved in 600 mL of AcOEt and 6 mL of H_2SO_4.

The solution was brought to approximately 77°C and left under stirring for 18 hours.

The solution was then washed with two 300-mL portions of saturated saline solution, with two portions of solution for extinguishing the oxidant (H_2O 100 mL, $Na_2S_2O_3$ 5 g, NaOH 5 g), with a 300-mL portion of a saturated aqueous solution of $NaHCO_3$, and again with a 300-mL portion of saline solution.

The organic phase was evaporated, recovering a red-coloured solid residue. The solid was then washed with two 80-mL portions of MeOH, to obtain, with this procedure, 75 g of product 2,5-dimethyl-3,4-diiodo-thiophene (yield 82%).

Stage b: synthesis of 2,5-dimethyl-3,4 *bis* (diethoxyphosphoryl)-thiophene

Into a 500-mL four-necked flask, provided with magnetic stirrer, thermometer, drip funnel and distillation apparatus, there were introduced, in a nitrogen atmosphere, 9.86 g of palladium acetate and 200 mL of $P(OEt)_3$.

To the solution, brought to 140°C, there were added by dripping, in approximately 2 hours, 40 g of 2,5-dimethyl-3,4-diiodo-thiophene, dissolved in 150 mL of $P(OEt)_3$. The solution was left under stirring at 140°C for a further 3 hours, and then the solvent was evaporated using a mechanical pump (46-105°C; 4 mmHg).

The oily residue recovered was extracted with five 100-mL portions of heptane, and the extracts were re-united and evaporated. There was obtained an oil, which was further purified by means of chromatography on silica gel (eluent AcOEt/EtOH 9/1). In this way, there were recovered 20 g of 2,5-dimethyl-3,4 *bis*(diethoxyphosphoryl)-thiophene (yield 48%). A sample was purified by distillation [boiling point = 170-175°C/ 3 torr (4 mbar)].

^{1}H-NMR: 4.15 ppm (m, 8H); 2.6 ppm (d, 6H); 1.3 ppm (t, 12H).

^{31}P-NMR: 12.5 ppm

The pure product was a colourless solid that crystallized from pentane

Stage c: synthesis of 2,5-dimethyl-3,4-*bis*(diphosphino)-thiophene

Into a 250-mL four-necked flask, provided with magnetic stirrer, thermometer and drip funnel, there were introduced, in a nitrogen atmosphere, 3.6 g of $LiAlH_4$ and 80 mL of THF.

The solution was brought to ~60°C, and 11.2 mL of $(CH_3)_3SiCl$ were added by means of a syringe. The suspension was then left under stirring for 2 hours at room temperature.

The mixture was cooled again to ~60°C, and there were dripped, in 20 minutes approximately, 5.6 g of 2,5-dimethyl-3,4 *bis*(diethoxyphosphoryl) thiophene dissolved in 20 mL of THF, and the solution was left under stirring at room temperature for 3 hours.

There were then added to the mixture, in order, 3.6 mL of H_2O, 3.6 mL of 15% NaOH, and again 10.8 mL of H_2O, and it was then left under stirring up to formation of a filterable precipitate.

After filtration, the precipitate was washed with four 20-mL portions of THF, and the solvent was evaporated.

The residue was refluxed with 50 mL of toluene and washed with two 20-mL portions of H_2O. The organic phase was filtered on dicalite and evaporated, to obtain with this procedure 2.5 g of crude 2,5-dimethyl-3,4-*bis*(diphosphino)-thiophene (yield > 90%). A sample of product was purified by distillation [boiling point: 70-75°C/5 torr (6.7 mbar)].

^{1}H-NMR: 4.2 ppm (t, 2H); 3.2 ppm (t, 2H); 2.5 ppm (s, 6H).

^{31}P-NMR: -155 ppm

The pure product is a colourless liquid.

Stage d: synthesis of (R,R) 2,5-dimethyl-[3,4 *bis*(2',5'-dimethylphospholanyl)]-thiophene)

Into a 250-mL four-necked flask, provided with magnetic stirrer, thermometer and drip funnel, there were introduced, in a nitrogen atmosphere, 0.47 g of 2,5-dimethyl-3,4-*bis*(diphosphino)-thiophene, 0.96 g of (S,S) 4,7-dimethyl-[1,3,2]dioxathiepane-2,2-dioxido, and 30 mL of THF.

The solution was brought to 10°C, and 7.5 mL of nBuLi (1.7 M) were added, in approximately 40 minutes, by means of a syringe. The mixture was then left under

stirring for 60 minutes at 10°C, and there were then added 2.5 mL of methanol. The solution was filtered, evaporated, and extracted with three 20-mL portions of heptane. The organic phases were re-united, filtered and evaporated, and the residue was washed with two 3-mL portions of MeOH.

With this procedure, there were recovered 0.46 g of (R,R) 2,5-dimethyl-[3,4 *bis*(2',5'-dimethylphospholanyl)]-thiophene) (yield: 50%).

^{1}H-NMR: 0.94 ppm (m, 6H, -CH_3); 1.17 ppm (m, 6H, -CH_3); 1.25-1.55 ppm (m, 4H);

2.0-2.2 ppm (m, 4H); 2.46 ppm (s, 6H, -CH_3); 2.4-2.6 ppm (m, 2H); 3.0- 3.1 ppm (m, 2H).

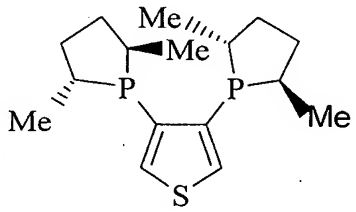
^{31}P-NMR: 4.1 ppm (s).

Mass (M^+): 340

$[\square]^{25}_D$ +54.2 (c = 1, chloroform)

redox potential (E°): 0.1 V

Example 2. Synthesis of (R,R) [3,4 *bis*(2',5'-dimethylphospholanyl)]-thiophene



Stage a: synthesis of 3,4-dibromo-thiophene

Br_2 (23.5 mL) was dripped into a solution of thiophene (31.6 g) in $CHCl_3$ (38 mL), at a temperature of 0°C under stirring, for an interval of 1 h 30 min. Next, Br_2 (10 mL) was added at room temperature. The mixture was heated under reflux for 3 h 30 min, and then NaOH 2N (57 mL) was added with caution, and the heating was prolonged for a further 30 min. The mixture was transferred into a beaker and cooled off to room temperature. The solid was gathered by filtration and washed with abundant water. After crystallization from $CHCl_3$, there were obtained 134.6 g of 2,3,4,5-tetrabromothiophene, which were slowly added by portions to a mixture, under stirring at 50°C, of 400 mL of H_2O, 107 g of powdered zinc and 600 mL of AcOH. The solution was left under stirring at a temperature of approximately 60°C

for 45 min and at room temperature for 12 h. The solution was diluted with water and extracted with CH_2Cl_2. The organic phase was washed with a saturated solution of $NaHCO_3$, with H_2O, and then dehydrated on Na_2SO_4. The solvent was evaporated, and the residue was distilled at reduced pressure [boiling point: 104-107°C, 22.5 torr (30 mbar)] to yield 3,4-dibromo-thiophene (53.5 g) (yield: 54%)

Stage b: synthesis of 3,4-*bis*(diethoxyphosphoryl)-thiophene

A suspension of $PdCl_2$ (0.15 g) in 3,4-dibromo-thiophene (2.0 g) was brought to the temperature of 115°C, and $P(OEt)_3$ (3.3 g) was then dripped under stirring, in an inert atmosphere, bringing the temperature of the bath to 130°C. Once dripping was completed, the clear yellow solution was heated to 160°C for 1 h 30 min. The mixture was diluted with CH_2Cl_2, washed twice with water, dehydrated, and the solvent was evaporated at reduced pressure. The residue underwent chromatography on silica gel by flash chromatography (AcOEt). The tail fractions (Rf: 0.15) were re-united, deprived of the solvent at reduced pressure to yield an oil, which was distilled under vacuum conditions in bubble apparatus [boiling point = 210°C / 0.5 torr (0.73 mbar)] to yield the 3,4-*bis*(diethoxyphosphoryl)-thiophene (1.3 g) as yellowish oil, which solidified at low temperature (yield: 54%)

m.p.: 28-30°C; ^{1}H-NMR: 1.2 ppm (m,12H); 4.1 ppm (m, 8H); 8.1 ppm (m, 2H);

^{31}P-NMR: 11 ppm (s);

^{13}C-NMR: 16 ppm (CH_3); 62 ppm (CH_2);

Mass (M^+): 356.

Stage c: synthesis of 3,4-*bis*(diphosphino)-thiophene

Trimethyl chlorosilane (0.94 mL) was added, in an inert atmosphere, to a suspension of $LiAlH_4$ in THF (7.4 mL, 1 M) at the temperature of 78°C and was left under stirring for 2h at room temperature. The solution was then brought to the temperature of 60°C, and there was dripped a solution of 3,4-diethylphosphonate (0.44 g) in THF (7.4 mL), and it was then left under stirring at room temperature for 2 h. The reaction was extinguished with MeOH (2.5 mL), cooling with an ice bath. The solvent was evaporated at reduced pressure, and the grey solid obtained was washed with degassed CH_2Cl_2 (approximately 15 mL). By evaporation of the

solvent, a yellowish residue was obtained, which was distilled in a bubble apparatus under vacuum conditions [boiling point = 80-90°C/ 0.2 torr (0.27 mbar), rejecting some low-boiling samples (boiling point = 50°C); 3,4-*bis*(diphosphino)-thiophene was obtained as a colourless oil, which was kept under argon at 10°C.

TLC: Rf = 0.5 (hexane);

^{1}H-NMR: 3.6-4.2 ppm (d, 4H); 7.5 ppm (m, 2H);

^{31}P-NMR: -148 ppm (s)

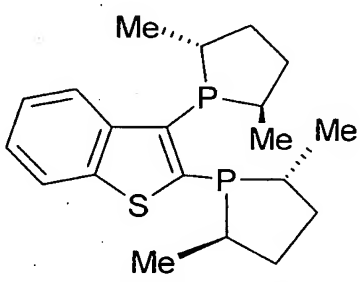
Stage d: synthesis of (R,R) 3,4 *bis*(2',5'-dimethylphospholanyl)-thiophene

Into a three-necked flask provided with magnetic stirrer, there were introduced, in a nitrogen atmosphere, 20.3 mg of 3,4-*bis*(diphosphino)-thiophene, 50 mg of (S,S) 4,7-dimethyl-[1,3,2]dioxathiepane-2,2-dioxido and 4 mL of THF. The solution was brought to 10°C, and 0.38 mL of nBuLi (1.6 M) were added in approximately 15 minutes by means of a syringe; the mixture was then left under stirring overnight. Then, the reaction was extinguished with 1 mL MeOH; after evaporation of the solvent, the residue was washed with two portions of MeOH, the solvent was again evaporated, and the solid obtained was washed with 10 mL of CH_2Cl_2. The oily residue, recovered by evaporation of the solvent at reduced pressure, underwent chromatography on silica gel (CH_2Cl_2-EtOH), to obtain 30 mg of (R,R) 3,4 *bis*(2',5'-dimethylphospholanyl)-thiophene.

^{1}H-NMR: 0.75 ppm (m, 6H, -CH_3); 1.22 ppm (m, 6H, -CH_3); 1.20-1.35 ppm (m, 4H); 1.8-2.1 ppm (m, 4H); 3.4 ppm (m, 2H); 7.5 ppm (m, 2H aromatic);

^{31}P-NMR: 13.1 ppm (s).

Example 3. Synthesis of (R,R) [3,4 *bis*(2',5'-dimethylphospholanyl)]-benzo[b]thiophene



Stage a: synthesis of 2,3-dibromo-benzo[b]thiophene

A solution of Br_2 (21.1 mL) in $CHCl_3$ (65 mL) was dripped into a solution of benzo[b]thiophene (26.4 g) in $CHCl_3$ (120 mL), under stirring, at a temperature of 0°C. The process of the reaction was controlled in TLC (hexane) up to the disappearance of the starting product: Rf (thianaphthene): 0.33 Rf (2,3-dibromobenzothiophene): 0.5. The mixture was then poured into aqueous NaOH; the organic phase was separated, washed twice with a solution of 10% NaOH and once with water, and then dehydrated on Na_2SO_4. The solvent was evaporated to yield the 2,3-dibromo-benzo[b]thiophene as a white solid (52 g) (yield: 90%).

Stage b: synthesis of 2,3-*bis*(diethoxyphosphoryl)–benzo[b]thiophene

A suspension of $PdCl_2$ (0.15 g) in 2.3-dibromothianaphthene (2.4 g) was brought to the temperature of 115°C, and $P(OEt)_3$ (3.3 g) was then dripped under stirring and in an inert atmosphere. Once dripping was completed, the red solution was brought to 160°C. After 1 h 30 min, the mixture was diluted with CH_2Cl_2, washed twice with water and dehydrated. The solvent was evaporated at reduced pressure to yield a residue that underwent chromatography on silica gel by flash chromatography (AcOEt), to yield 2,3-*bis*(diethoxyphosphoryl)-benzo[b]thiophene (1.6 g) (yield: 60%).

m.p.: 67°C;

^{1}H-NMR: 1.4 ppm (m, 12H); 4.2 ppm (m, 8H); 7.4 ppm (m, 2H); 7.85 ppm (m, 1H); 8.5 ppm (m, 1H);

^{31}P-NMR: 9.0 ppm; 9.6 ppm

Stage c: synthesis of 2,3-*bis*(phosphino)–benzo[b]thiophene

Trimethyl chlorosilane (0.94 mL) was added, in an inert atmosphere, to a suspension of $LiAlH_4$ in THF (7.43 mL, 1 M) at a temperature of -78°C and was left under stirring for 2 h at room temperature. The solution was then brought to a temperature of -60°C, and a solution of 3,4-diethylphosphonate (0.5 g) in THF (7.43 mL) was dripped, and it was left under stirring at room temperature for 2 h. The reaction was extinguished with MeOH (2.5 mL), cooling with an ice bath.

The solvent was evaporated at reduced pressure, and the grey solid obtained was washed with degassed CH_2Cl_2 (approximately 15 mL). By evaporation of the

solvent, a yellowish oil was obtained, which underwent chromatography on silica gel in an inert atmosphere (Rf: 0.6, hexane). The 2,3-*bis*(phosphino)–benzo[b]thiophene obtained as solid, after evaporation of the solvent, was kept under argon at 20°C.

^{1}H-NMR: 3.6 ppm (s, 2H-P); 4.7 ppm (s, 2H-P); 7.4 ppm (m, 2H); 7.9 ppm (m, 2H);

^{31}P-NMR: -162.6 ppm

Stage d: synthesis of (R,R) 3,4 *bis*(2',5'-dimethylphospholanyl)-benzo[b]thiophene

A 1.6 M solution in hexane of BuLi (0.12 mL) was dripped into a solution of diphosphine (18 mg) in THF (1.6 mL), and the (orange) solution was left under stirring for 1 h 30 min. There were then dripped 33.2 mg of cyclic sulphate of (2S,5S)-hexanediol dissolved in 2 ml of THF, and the solution turned pale yellow. It was left under stirring for 2 h. An 1.6 M solution in n.hexane of BuLi (0.13 mL) was dripped to bring about closing of the phospholanic ring, and the solution once again became orange.

After leaving under stirring for 2 h, the disappearance of the starting product was controlled in TLC (hexane), and the disappearance of the cyclic sulphate was controlled in TLC (AcOEt). The mixture was left under stirring overnight in an inert atmosphere; then the reaction was extinguished with MeOH (0.5 mL), and the solvent was evaporated at reduced pressure. The solid was washed with degassed CH_2Cl_2, and the filtrate was concentrated at reduced pressure. A solid was obtained, which underwent chromatography on silica gel (EtOH). By evaporating the solvent, the product was obtained as a pale-yellow solid.

melting point: 174°C

^{1}H-NMR: 0.75 ppm (m, 6H, -CH_3); 1.22 ppm (m, 6H, -CH_3); 1.20-1.35 ppm (m, 4H);

1.8-2.1 ppm (m, 4H); 3.7 (m, 4H); 7.3 ppm (m, 4H aromatic).

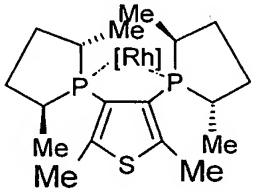
^{31}P-NMR: ???-8.55 ppm (s).

Mass (M^+): 362

$[\square]^{25}_D$ +24.8 (c = 1.39, methylene chloride)

redox potential (E°): P_1 0.4 V; P_2 0.65 V

Example 4. Preparation of the complex {Rh(COD) (R,R) 2,5–dimethyl-[3,4 *bis*(2',5'-dimethylphospholanyl)]-thiophene}BF_4

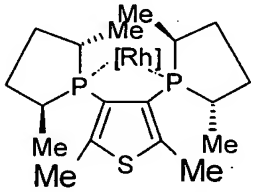


[Rh] = Rh(COD)BF_4

A mixture of 96.7 mg of $[Rh(COD)_2]BF_4$ prepared according to Inorg. Chem. 24, 2334 (1985) and 90 mg of (R,R) 2,5–dimethyl-[3,4 *bis*(2',5'-dimethylphospholanyl)]-thiophene, prepared according to Example 1, in 10 mL of degassed methylene chloride was kept under stirring at room temperature for 2 h. There was then added 5 mL of degassed THF to the mixture, and then slowly 10 mL of degassed hexane, subsequently concentrated up to start of crystallization and then kept at -20°C overnight. The dark-red solid was filtered, washed twice with 3 mL of hexane, and finally dried under vacuum conditions. There were obtained 32.5 mg of catalyst. A further 120 mg, of comparable chemical purity on the basis of the NMR spectra, were recovered by concentration from the mother liquor.

^{31}P-NMR: 51 ppm (d, J = 160.5 Hz).

Example 5. Preparation of the complex {Rh(COD) (R,R) 2,5–dimethyl-[3,4 *bis*(2',5'-dimethylphospholanyl)]-thiophene} OTf

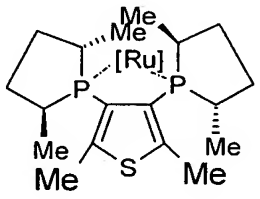


[Rh] = Rh(COD)OTf

A mixture of 108.9 mg of $[Rh(COD)_2]OTf$, prepared according to Inorg. Chem. 24, 2334 (1985) and 88 mg of (R,R) 2,5-dimethyl-[3,4 *bis*(2',5'-dimethylphospholanyl)]-thiophene, prepared according to Example 1, in 10 mL of degassed methylene chloride was kept under stirring at room temperature for 2 h. The mixture was concentrated up to approximately 40% of the initial volume, and 6 mL of degassed

THF and of 4 mL of degassed hexane were added, up to start of crystallization, and it was then kept at -5/10°C for 30 min. The orange-red solid was filtered, washed three times with 4 mL of hexane, and finally dried under vacuum conditions. Approximately 100 mg of catalyst were obtained.

Example 6. Preparation of the complex {Ru I(p. cymene) (R,R) 2,5-dimethyl-[3,4 *bis*(2',5'-dimethylphospholanyl)]-thiophene} I

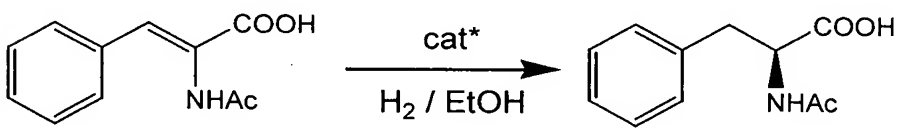


[Ru] = RuI(p.cimene)I

In a four-necked 100-mL flask, provided with coolant, valve for nitrogen, and magnetic stirrer, there were introduced under nitrogen flow, 144 mg of $[RuI_2(pCym)]_2$ and 100 mg of (R,R) 2,5-dimethyl-[3,4 *bis*(2',5'-dimethylphospholanyl)]-thiophene, prepared according to Example 1. There were then added 25 mL of CH_2Cl_2 and 9 mL of degassed MeOH, and the solution was refluxed for two hours. The solvent was evaporated, recovering as residue the catalyst as a dark-red crystalline solid.

^{31}P-NMR: 79.3 ppm (d, J = 45.8 Hz); 59.9 ppm (d, J = 45.8 Hz).

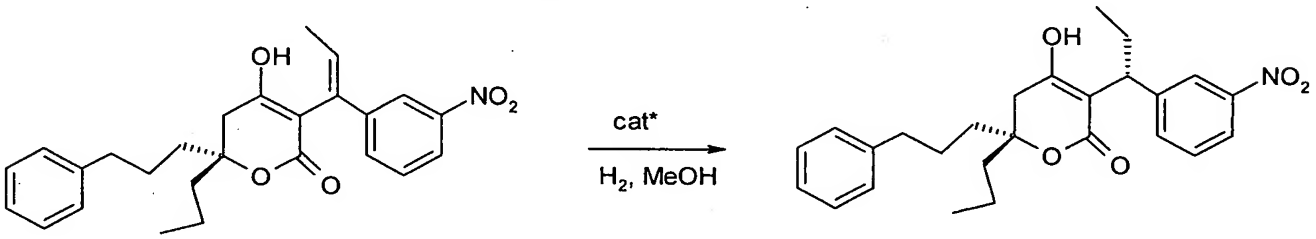
Example 7. Hydrogenation of *N*-acetamide cinnamic acid



In a nitrogen atmosphere, 0.7 g (3.4 mmol) of *N*-acetamide cinnamic acid were dissolved in 100 mL of degassed EtOH, and 11 mg (0.017 mmol) of catalyst,

prepared according to Example 4, were weighed in a nitrogen atmosphere.
The mixture was charged into an 250-mL autoclave in an argon atmosphere. Three cycles of washing with Ar were then carried out, followed by three cycles of washing with H_2. Then, the autoclave was pressurized at 3.5 bar.
The mixture was kept under stirring at room temperature for 1.5 hours. With this procedure a 100% conversion was obtained, and an enantiomeric excess of 97% of *N*-acetyl-phenylalanine.

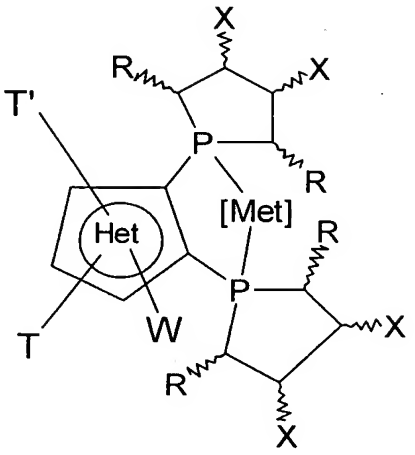
Example 8. Hydrogenation of [6(R)]5,6-dihydro-4-hydroxy-3-[(Z)-1-(3-nitrophenyl) propenyl]-6-[1-(2-phenyl)ethyl]-6-propyl-2H-piran-2-one



In a nitrogen atmosphere, 0.8 g (1.9 mmol) of [6(R)]5,6-dihydro-4-hydroxy-3-[(Z)-1-(3-nitrophenyl)propenyl]-6-[1-(2-phenyl)ethyl]-6-propyl-2H-piran-2-one were dissolved in 100 mL of degassed MeOH, and 14 mg (0.019 mmol) of catalyst prepared according to Example 5 were weighed under nitrogen.
The mixture was charged into a 250-mL autoclave in an argon atmosphere. Three cycles of washing with Ar were then carried out, followed by three cycles of washing with H_2. Then, the autoclave was pressurized at 5 bar.
The mixture was kept under stirring at room temperature for 20 hours. With this procedure, a 100% conversion was obtained, with a diastereoisomeric excess of [3 (R),6(R)]5,6-dihydro-4-hydroxy-3[1-(3-nitrophenyl)propyl]-6-[1-(2-phenyl)ethyl]-6-propyl-2H-piran-2-one corresponding to 91%.

CLAIMS

Metallic catalysts of the formula (I)



(I)

where:

[Met] is a metal chosen from among those of the group Ru, Rh, Ir, Pt, Pd, Ni, Re, and Cu, having a state of oxidation n, where n is 0, +1, +2 or +3, and containing possible ancillary co-ligands for completing its state of valence;

represents an aromatic pentatomic heterocycle, containing at least one hetero-atom chosen from among oxygen, sulphur and nitrogen;

T and T', which are the same as or different from one another, are chosen from among hydrogen, a linear C1-C10 alkyl, either cyclic or branched, hydroxyalkyl, alkoxyalkyl, phenyl, alkylphenyl, naphthyl, alkoxyphenyl, dialkylaminophenyl, carboxyphenyl, carbalkoxyphenyl, or else T and T', taken together, constitute an aromatic carbocyclic ring, possibly substituted by one or more alkyl, hydroxy, alkoxy, dialkylamino, carboxy, carbalkoxy or sulphonic groups;

W is a substituent present only when the hetero-atom is nitrogen and is chosen from among H, a linear C1-C10 alkyl, either cyclic or branched, alkoxyalkyl, phenyl, alkylphenyl, naphthyl, alkoxyphenyl, dialkylaminophenyl, carboxyphenyl,

carbalkoxyphenyl;

R is chosen from among hydrogen, a linear C1-C10 alkyl, either cyclic or branched, hydroxyalkyl, alkoxyalkyl, phenyl, alkylphenyl;

X is chosen from among H, a linear C1-C10 alkyl, either cyclic or branched, hydroxy, alkoxy, benzyloxy, acyloxy, O-tetrahydropyranyl, O-tetrahydrofuranyl, or else where the two substituents X, taken together with m carbon atoms bound thereto, with m = 1, 2 or 3, form a carbocyclic ring with a total of 5-7 atoms or a saturated heterocyclic ring with 5-7 atoms.

2.The catalysts according to Claim 1, characterized in that they are in racemic form.

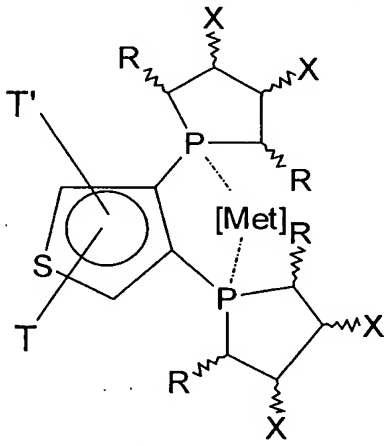
3.The catalysts according to Claim 1, characterized in that they are in meso form.

4. The catalysts according to Claim 1, characterized in that they are in enantiomerically enriched form of configuration R or S with the limitation, that:

a) the carbon atoms in positions 2' and 5' of the phospholanic rings possess the same absolute configuration with respect to one another;

b) the carbon atoms in positions 3' and 4' of the phospholanic rings possess the same absolute configuration with respect to one another.

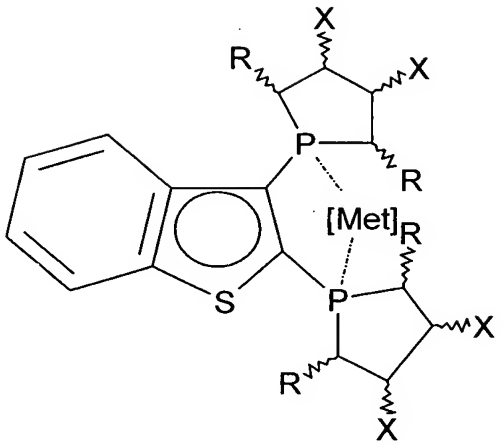
5. The catalysts, according to any one of Claims 1-4, of formula (V)



(V)

in which T, T', R, X and [Met] have the meanings indicated above.

6. The catalysts, according to any one of Claims 1-4, of formula (VI)

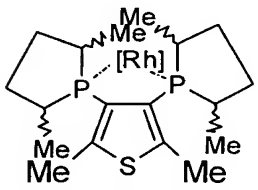


in which R, X and [Met] have the meanings indicated above.

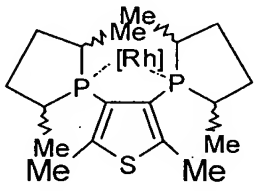
(VI)

7. The catalysts according to Claim 5, characterized in that T and T' are both H or both methyl.

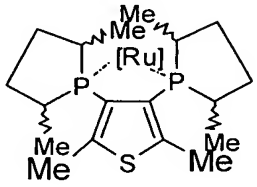
8. The catalysts according to Claim 5, chosen in the group consisting of:



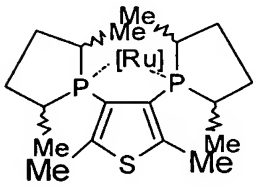
[Rh] = $Rh(COD)BF_4$



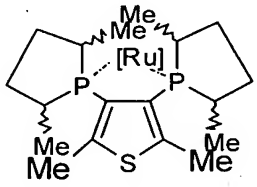
[Rh] = Rh(COD)OTf



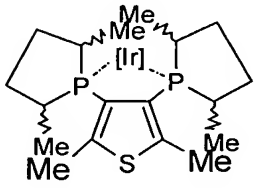
[Ru] = RuI(p.cimene)I



[Ru] = Ru(bis metallil)



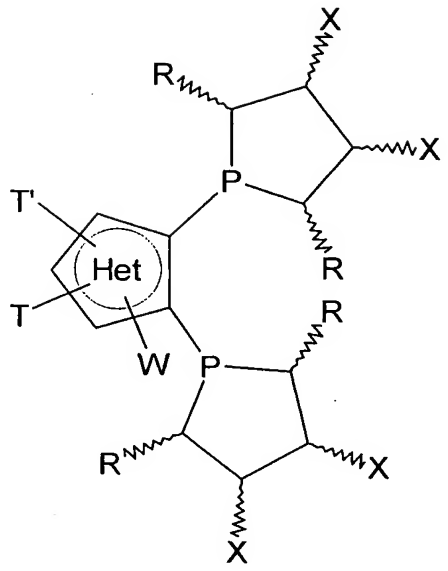
[Ru] = RuX_2



[Ir] = Ir(COD)OTf

where the two stereocentres in positions 2' and 5' of the phospholanic rings have both absolute configuration (R) or both absolute configuration (S).

9. Ligands with an ortho *bis*(1-phospholanyl)heteroarenic structure of formula (IA)



(IA)

in which

represents an aromatic pentatomic heterocycle, containing at least one hetero-atom chosen from among oxygen, sulphur and nitrogen;

T and T', which are the same as or different from one another, are chosen from among hydrogen, a linear C1-C10 alkyl, either cyclic or branched, hydroxyalkyl, alkoxyalkyl, phenyl, alkylphenyl, naphthyl, alkoxyphenyl, dialkylaminophenyl, carboxyphenyl, carbalkoxyphenyl, or else T and T' taken together constitute an aromatic carbocyclic ring possibly substituted by one or more alkyl, hydroxy, alkoxy, dialkylamino, carboxy, carbalkoxy or sulphonic groups;

W is a substituent present only when the hetero-atom is nitrogen and is chosen from among H, a linear C1-C10 alkyl, either cyclic or branched, alkoxyalkyl,

phenyl, alkylphenyl, naphthyl, alkoxyphenyl, dialkylaminophenyl, carboxyphenyl, carbalkoxyphenyl;

R is chosen from among hydrogen, a linear C1-C10 alkyl, either cyclic or branched, hydroxyalkyl, alkoxyalkyl, phenyl, alkylphenyl;

X is chosen from among H, a linear C1-C10 alkyl, either cyclic or branched, hydroxy, alkoxy, benzyloxy, acyloxy, O-tetrahydropyranyl, O-tetrahydrofuranyl, or else where the two substituents X, taken together with m carbon atoms bound thereto, with m = 1, 2 or 3, form a carbocyclic ring with a total of 5-7 atoms or a saturated heterocyclic ring with 5-7 atoms.

10. The ligands according to Claim 9, characterized in that they are in racemic form.

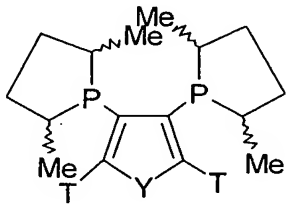
11. The ligands according to Claim 9, characterized in that they are in meso form.

12. The ligands according to Claim 9, characterized in that they are in enantiomerically enriched form of configuration R or S with the limitation, that:

a) the carbon atoms in positions 2' and 5' of the phospholanic rings possess the same absolute configuration with respect to one another;

b) the carbon atoms in positions 3' and 4' of the phospholanic rings possess the same absolute configuration with respect to one another.

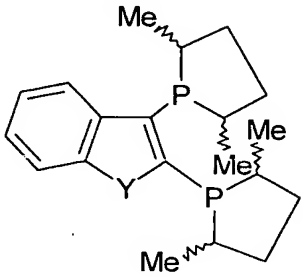
13. The ligands according to any one of Claims 9-12, characterized in that they have the following formula (II)



(II)

and in which Y is chosen from among O, S and N(W), T and W are chosen from among hydrogen and methyl, and where the carbon atoms in positions 2' and 5' of the phospholanic rings have both absolute configuration (R) or both absolute configuration (S).

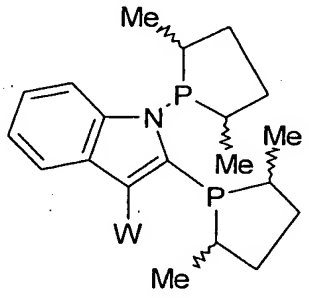
14. The ligands according to any one of Claims 9-12, characterized in that they have the following formula (III).



(III)

in which Y is chosen from among O, S and N(W), T and W are chosen from between hydrogen and methyl, and where the carbon atoms in positions 2' and 5' of the phospholanic rings have both absolute configuration (R) or both absolute configuration (S).

15. The ligands according to any one of Claims 9-12, characterized in that they have the following formula (IV).



(IV)

and in which W is chosen from between hydrogen and methyl and where the carbon atoms in positions 2' and 5' of the phospholanic rings have both absolute configuration (R) or both absolute configuration (S).

16. A process of preparation of the catalysts according to any one of Claims 1-8, comprising the [Met] reaction in which [Met] has the aforesaid meanings with the ligands according to any one of Claims 9-15.

17. Use of the catalysts according to any one of Claims 1-8 in chemoselective

syntheses.

18. Use of the catalysts according to any one of Claims 1-8 in regioselective syntheses.

19. Use of the catalysts according to Claims 1, 4 or 8 in stereoselective syntheses.

20. Use according to Claim 19, in which said stereoselective syntheses are chosen in the group consisting of hydrogenation of C=C, C=O, C=N groups, of isomerization of enamines and of formation of C-C bonds,

21. Use according to Claim 20, in which said reactions of C-C formation are chosen in the group consisting of the Heck reaction, the Diels-Alder reaction, allylic substitution and aldolic condensation.

Milan, date

f. CHEMI S.p.A.

The Representative

(signature)

Dr. Gemma Gervasi

of NOTARBARTOLO & GERVASI S.p.A.

DECLARATION UNDER 37 CFR 1.68

I, Giovanna Luisa Sarolo, declare

That I reside at Via Podgora 6, Milan, Italy;

That I am familiar with the Italian and English languages;

That I am a Sworn Translator, appointed by the Court of Milan, Italy;

That I have prepared the attached translation of the Italian Patent Application No. **MI2002A000415** filed on **01 March 2002** with the title: "Metallic Catalysts for Chemo-, Regio-, and Stereoselective Reactions, and Corresponding Precursors" , said Italian language document being already filed at WIPO during the PCT procedure.

That the attached translation is complete and accurate and fairly reflects the meaning and content of said Italian language document.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such wilful false statements may jeopardize the validity of the application or any patent issued thereon.

Giovanna Luisa SAROLO

Milan, ITALY, 6 July 2007